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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/814,661 | 03/22/2001 | Rodney Rothstein | 56615-A-PCT-US/JPW/AJM/WW | 2135 |

7590 11/18/2005

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| EXAMINER | |
|---|---|
| CANELLA, KAREN A | |
| **ART UNIT** | **PAPER NUMBER** |
| 1643 | |

DATE MAILED: 11/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/814,661 | ROTHSTEIN ET AL. | |
| | Examiner | Art Unit | |
| | Karen A. Canella | 1643 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☐ Claim(s) *14,15 and 17-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *14, 15 and 17-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

Claim 15 has been amended. Claims 14, 15 and 17-19 are pending and under consideration.

The rejection of claims 14, 15 and 17-19 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of screening for a compound that is capable of reducing the division rate of a yeast cell comprising contacting the yeast cell with a fragment of the SML1 protein or a peptidomimetic of the SML1 protein, and measuring the division rate of the cell in comparison to a cell in the absence of said fragment or peptidomimetic to identify a compound capable of reducing the division rate of the cell, does not reasonably provide enablement for a method of screening for a the broadly claimed compounds or a method of screenign in cells other than yeast cells is maitained for reasons of record. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims..

(A) As drawn to cells other than yeast cells

The claims are broadly drawn to encompass the reduction of cell growth in any type of cell. The specification states that "The search in the database reveals no other homologue in yeast or in any other organisms". Thus, as of the filing date, SML1 was only to be found in yeast cells. Thus one of skill in the art would not have a reasonable expectation of success of finding a mammalian homologue or any other homologue of SML1 which was present in cells other than yeast. The specification teaches that the SML1 protein binds directly to the large subunit of ribonucleotide reductase in yeast, and that the presence of said SML1 protein inhibits dNTP synthesis post-transcriptionally. The art teaches that peptides derived from the carboxyl terminus of the small subunit of ribonucleotide reductase (RR2 or rnr2) can act as an antagonist of the interaction between the large subunit (RR1 or rnr1) and the small subunit (Cohen et al, Nature, 1986, Vol. 321, pp. 441-443, especially page 442, second column, line 13 to page 443, first column, line 8) in herpesvirus encoded ribonucleotide reductase, thus inhibiting the synthesis of dNTP (ibid, page 332, first column, lines 8-10). It is specifically noted that the peptides derived from the herpesvirus encoded ribonucleotide reductase failed to inhibit the cellular ribonucleotide reductase and there was no sequence similarity between the carboxyl terminus of the RR2 subunit of herpesvirus and mammalian RR2. It appears that the sequences

of various ribonucleotide reductases differ substantially between organisms and it would not be expected that a protein which interacts with the a particular subunit in a specific organism would be able to interact with the same subunit in a different organism. It would be reasonably to conclude that the SML1 protein of the instant invention (SEQ ID NO:2) would not be able to bind to the large subunit of mammalian ribonucleotide reductase. Furthermore, because a homologues of SML1 are not known to exist, the instant method could only be carried out with SML1 of yeast in yeast cells because there would be no reasonable expectation that the SML1 of SEQ ID NO:2 would bind to the large subunit of ribonucleotide reductase on human cells or mammalian cells and inhibit the interaction of RR1 with RR2.

(B) As drawn to mimetics of SML1 other than fragments of SML1 and peptidomimetics

The instant claims encompass the screening of compounds of any type including small molecule synthetic drugs, and natural products, as evidenced by claim 15. In order to fulfill the requirements of 112, first paragraph, the specification should enable the determination of whether or not said compounds are able to reduce the division rate of a cell by mimicking the binding of the SML1 protein to the large subunit of ribonucleotide reductase. The prior art teaches the inhibition of binding of the RR1 subunit to the RR2 subunit of ribonucleotide reductase by peptides derived from the carboxyl terminus of RR2, and that small peptide mimetics can increase the inhibition of enzyme activity to a greater extent than the sequence of the peptide fragment that retains the wild type sequence of the RR2 subunit (Dutia et al, Nature, 1986, Vol. 321, pp. 439-441, especially page 440, second column, lines 7-22). This lends credence to the existence of peptidomimetics which can inhibit the binding of SML1 to the large subunit of ribonucleotide reductase, and provides a nexus for how to find said peptidomimetics. However, neither the specification nor the prior art describe the structural characteristics of compounds which are not peptides which can inhibit the binding of SML1 to the large subunit of ribonucleotide reductase, nor has the specification provided a single example of a non-peptide compounds which can function as claimed. Therefore, the instant methods claim which relies on the existence of "organic compounds" and "synthetic compounds" which are not peptides is not enabled by the specification, because one of skill in the art is not given any guidance which would lead to the identification of an "organic compound" or a "synthetic compound" which is not a peptide. Further, one of skill in the art would not have a reasonable expectation of success

carrying out the assay for the instant compounds because the existence of said compounds at the time of the instant filing date is uncertain.
Given the lack of teachings in the specification addressing the issues of sections A and B above, one of skill in the art would be subjected to undue experimentation without reasonable expectation of success in order to practice the instant method to the full extent of the claims.

Applicant argues that it was recognized at the time of filing that yeast SML1 interacted with mammalian RR and has provided the paper of Chabes et al to support this allegation. This has been considered but not found persuasive. The specification must be enabling at the time at which the earliest filing date is sought: in this case, the earliest filing date is September 24, 1998. The paper of Chabes et al was published December 17, 1999. It is further noted that said paper states "the inhibition as seen in and in vitro mouse RR assay is less pronounced than in the yeast system, which indicated an inhibition mechanism different from the one in yeast". Thus, one of skill in the art could not be certain that peptides derived from the carboxyl terminus of the small subunit of ribonucleotide reductase (RR or rnr2) can act as an antagonist of the interaction between the large subunit and the small subunit as disclosed by Cohen et al, ibid, to occur in yeast because it appears from the disclosure of Chabes et al that the mechanism of inhibition between SML1 and mammalian RR differs from the inhibition occurring between SML1 and yeast RR.

Applicant argues that amendment of claim 15 to cancel reference to "an organic compound" and a "synthetic compound" would render moot the rejection based on the broadly invoked "compounds". This has been considered but not found persuasive. Although this subject matter was canceled in dependent claim 15, claim 14 contains no limitation on the term "compound".

All other rejections and objections are withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 11 am to 10 pm, except Wed, Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
11/14/2005